Formulation Optimization and Evaluation of Nanostructured Lipid Carriers Containing Valsartan

Ravish J. Patel and Zil P. Patel

Department of Pharmaceutics & Pharmaceutical Technology, Ramanbhai Patel College of Pharmacy, Charotar University of Science & Technology, Changa, Anand, India.

Received November 15, 2012; accepted March 17, 2013

ABSTRACT

Nanostructured lipid carriers (NLCs), a lipid based colloidal carrier system, offer many advantages such as increase the solubility, improves the bioavailability and therapeutic efficacy. Incorporation of liquid lipid can improve the drug loading capacity in the NLCs. Valsartan is an antihypertensive drug with low oral bioavailability ranging from 10-35% because of poor solubility and extensive first pass hepatic metabolism. The purpose of present study was to develop and characterize the valsartan loaded nanostructured lipid carriers (Val-NLCs) to enhance the solubility, bypass the hepatic first-pass metabolism, and enhance the lymphatic absorption leading to greater oral bioavailability. Valsartan loaded NLCs were prepared by melt emulsification method and optimized using a two level full factorial design. Effect of content of Capmul MCM EP on crystallinity of tristearin was studied by differential scanning calorimetry (DSC) method. The particle size, entrapment efficiency, drug loading and zeta potential values of optimized batch were 62±0.494 nm, 86.59±0.671, 8.65±0.06 % and -17.4 mV, respectively. TEM images showed spherical particles with diameter of around 50 nm. In vitro drug release of 70% was observed at the end of 12 hrs. Ex-vivo drug release of 90% was observed in 2 hrs. Stability study indicated that the prepared Val-NLCs suspension was stable at refrigerator conditions for one month. Lyophilization produced free flowing Val-NLCs powder from suspension and was easy to reconstitute. Based on these results, it is concluded that NLCs are promising drug delivery for improving the oral bioavailability of valsartan.

KEYWORDS: Lipid nanoparticles; Nanostructured lipid carriers; Valsartan; Factorial design; Drug release.

Introduction

Lipid nanoparticles (LNrs) have gained immense attention since last few years as they avail the combined benefits of both lipids and nano-sized particles. LNrs are considered to be a safer alternative to polymeric nanoparticles owing to their biodegradable and biocompatible nature. Thus the LNrs are preferred for oral administration of drugs with poor solubility and low bioavailability. Oral route is one of the most preferred routes of drug administration especially for people with chronic diseases. Oral dosage forms are easy to administer and show good patient compliance. They are easy to manufacture economically on large scale. LNrs play a very important role in bioavailability enhancement of poorly soluble drugs (Muchow et al., 2008, Fricker 2010, Das, 2011). Lipids not only increases their solubility but also increases the absorption by Trojan horse effect (Pardridge, 2008). Among the various lipid nano systems known, only the Microemulsions (Sandimmun Neoral®), a microemulsion formulation of cyclosporine-A by Novartis) and Nanostructured Lipid Carriers (NLCs, cosmetic products by Pharmasol) have made their way to the commercial market.

Valsartan is an angiotensin II receptor blocker (ARB) widely used in the treatment of hypertension and cardiac failure(Yamamoto et al., 2012). The oral bioavailability of valsartan (tablet, capsule) is 23% (10–35%) (Flesch, 1996; Siddiqui and Husain, 2011). The poor bioavailability is due to its poor solubility (Mbah, 2005) and a significantly high first pass metabolism (Flesch, 1996; Bisessor, 2007). It is a weakly acidic drug and thus exhibits pH dependent solubility (Flesch, 1996). Many approaches have been made to improve the solubility and thus the bioavailability of valsartan since last decade, which includes complexation with hydroxyl propyl beta-cyclodextrins (Cappello, 2005), preparation of spherically agglomerated solid dispersions of valsartan (Tapas, 2010), solid dispersion with gelucire-50/13 and aeroperl-300 pharma and skimmed milk powder as carrier (Kumar, 2009; Shrivastava et al., 2009), solid dispersions with poloxamer 407 (Park, 2010) / poloxamer 188 (Sharma and Jain, 2010), valsartan-loaded gelatin microcapsule (Li, 2010) and crystalline salt forms of valsartan (Marti, 2005). Kavimandan and colleagues prepared an extended release gastro-retentive drug delivery system using swellable polymers - cellulose and...